Fetal Ventriculomegaly: Investigating Additional Brain Abnormalities by using MR Imaging

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ABSTRACT

Background and Purpose: Fetal ventriculomegaly (VM), is known to have a prevalence of association with other brain abnormalities. By using in utero MR imaging (iuMR), we aimed to determine the prevalence of brain abnormalities other than VM and investigate the hypothesis that the prevalence of having additional brain abnormalities (ABA) increases with the degree of VM.

Materials and Methods: We reviewed iuMR images of 75 fetuses. The enlarged ventricles were graded as mild (≤ 12mm), moderate (> 12 to ≤15mm), and severe (> 15mm). Prevalence of having ABA were calculated and compared among groups with different grades of VM.

Results: ABA was shown in 67% of fetuses. The most frequent ABA was agenesis of the corpus callosum. The prevalence of having ABA increased with the degree of fetal VM in all groups. Severe VM was associated with a higher prevalence of ABA when compared with mild VM in the prevalence of having ABA being present when compared with mild VM.

Conclusions: The prevalence of having ABA increases with the degree of fetal VM. Caution should be exercised that this trend of ABA does not apply to those fetuses with isolated VM by sonography due to the different subjects studied.

In utero MR imaging (iuMR) has been used in recent years as a complementary imaging modality for the examination of fetal brain [5, 6]. iuMR provides good soft-tissue characterization with multiplanar imaging capabilities, thus better delineation of structural brain abnormalities, when compared with antenatal sonography with limitations such as difficult visualization of the posterior fossa or the side of the brain near the transducer, or poor visualization of the fetus owing to maternal body habitus or oligohydramnios [7]. Neurological prognosis of fetal VM can be highly varied, ranging from excellent neurological status in isolated VM to VM associating with severe brain abnormalities [8].

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In this retrospective review of a cohort of fetal VM, identified by using iuMR examination, we aimed to determine prevalence of additional brain abnormalities (ABA) and determine the relationship between the degree of VM and prevalence of having ABA. We investigated the hypothesis that the prevalence of having ABA increased with the degree of VM.

MATERIALS AND METHODS

Patients
We reviewed MRI data in 75 fetal patients with finding of ventriculomegaly, selected from our iu MRI database in a period of 7 years starting from 2003. All patients were referred from our obstetricians. We rounded the gestational age (GA) of the subjects to the lower nearest week if the GA was greater than that week by three or fewer days. If the GA was greater than the lower nearest week by four or more days, we rounded the GA to the higher nearest week.

MR imaging
All fetuses were imaged with a 1.5-T MR unit (Intera; Philips Medical Systems, Best, the Netherlands). Images of the head in sagittal, coronal, and transverse planes were obtained with balanced fast field echo sequence (bFFE) (repetition time/echo time 4.4ms/2.2ms, flip angle of 80°, slice thickness of 4mm without gap, and matrix of 256 × 256) and images in sagittal and coronal planes were obtained with single-shot turbo spin-echo sequence (SShTSE) (repetition time/echo time of 600-800ms/60ms, flip angle of 90°, slice thickness of 5 mm without gap, and matrix of 256 × 256).

Image interpretation
Institutional review board approval was obtained for this cross-sectional retrospective study. Informed consent for MR imaging was obtained from all mothers. All the iuMR images were reviewed for the purposes of this study by two investigators, one of whom having a 10-year experience of iuMR brain studies. Each fetus was measured at one time point. The size of the lateral ventricles was determined by measuring the transverse diameter of the trigone on iuMR images on an axial view or a coronal view. The enlarged ventricles were graded as mild (≤ 12mm), moderate (> 12 to ≤ 15mm), and severe (> 15mm). The grading of VM of a subject was represented by the largest grading of the ventricles if the enlarged ventricles were asymmetrical. Brain abnormalities additional to VM (ABA) were recorded. The proportion of subjects with ABA was expressed as percentages. The fetuses were divided into two groups for further analysis according to the GA of the fetus at the time of iuMR imaging: 18-24 weeks' group and ≥25 weeks' group. The prevalence of having ABA in a group was the percentage of subjects with brain abnormality additional to VM. We also described the relationship between the prevalence of ABA and the grading of VM.

RESULTS

ABA was found in 50/75 (66.7%). The ABA consisted of Dysgenesis of corpus callosum (DCC) (n= 15, 30%) (Fig. 1), encephalomalacia or periventricular leukomalacia (PVL) (n=14, 28%) (Fig. 2), holoprosencephaly (HPE) (n= 4, 8%) (Fig. 3), germinal matrix hemorrhage (GMH) (n=3, 6%) (Fig. 4), Dandy-Walker spectrum (DWS) (n=3, 4%) (Fig. 5), Chiari malformation (n=2, 4%) (Fig. 6), meningocele or encephalcele (n=2, 2%), arachnoid cyst (n= 3, 6%), hemimegalencephaly (n= 1, 2%) (Fig. 7), cystic tumor (n=1, 2%) (Fig. 8), and aqueductal stenosis (n=2, 4%) (Fig. 9).

Nineteen to 24 Weeks’ Group
The median GA at the time of iuMR in this group was 23 weeks. ABA was identified in 14/24 (58.3%) fetuses in this age group. The categories of enlarged trigones in the 24 confirmed VM in fetuses of 19 –24 weeks’ gestational age, according to iuMR, were the following: mild, 4/24; moderate, 12/24; and severe, 8/24. ABA was shown in 14 fetuses of this subgroup (Table 1). Encephalomalacia (3/14) was the most frequently found abnormality in fetuses with VM in this age group.

Figure 1
Coronal T2-weighted image shows absence of the corpus callosum, suggesting agenesis of corpus callosum.
Figure 2. Coronal T2-weighted image shows periventricular hyperintensity around enlarged bilateral frontal horns, suggesting periventricular leukomalacia.

Figure 3. Coronal single-shot rapid acquisition T2-weighted image shows well-separated interhemispheric fissure but non-separation of the basal ganglia, suggesting semilobar holoprosencephaly.

Figure 4. Coronal single-shot rapid acquisition T2-weighted image shows increased T2 signal along right lateral ventricle with focal dilatation, consistent with sequel of germinal matrix hemorrhage.

Figure 5. Sagittal T2-weighted image shows enlarged posterior fossa with small hypoplastic vermis, suggesting Dandy-Walker Syndrome.
Fetal ventriculomegaly

Figure 6. Sagittal T2-weighted image shows small crowded posterior fossa with cerebellum herniating through foramen magnum, suggesting Chiari malformation.

Figure 7. Axial T2-weighted image shows enlargement of the left cerebral hemisphere with indistinct cerebral cortex, suggesting hemimegalencephaly.

Figure 8. Sagittal single-shot rapid acquisition T2-weighted image shows a posterior fossa cystic mass.

Figure 9. Coronal single-shot rapid acquisition T2-weighted image shows asymmetrically dilated bilateral ventricles with normal sized 4th ventricle, suggesting aqueductal stenosis.
Fetal ventriculomegaly

Twenty-five-weeks' and above Group

The median GA at the time of iuMR for this group was 30.5 weeks. Thirty-six of 51 (70.6%) fetuses had ABA. The categoric assessment of the largest trigone in the 51 cases of confirmed VM according to iuMR was the following: mild, 10/51; moderate, 16/51; and severe, 25/51. ABA was shown in 36 fetuses of this subgroup (Table 1). Dysgenesis of corpus callosum (DCC) (36.1%) was the most frequently associated developmental abnormality of the \( \geq 25 \) weeks’ group. Most fetuses had severe VM.

DISCUSSION

Fetal VM is associated with an increase in fetal and neonatal morbidity and mortality. In mild VM (atrial diameter of 10-15 mm), about 20% of subjects had developmental delay in the first year after birth [9]. A higher likelihood of developmental delay was observed in subjects with associated anomalies, when compared with those without anomalies [10]. The outcome of fetal VM has been reported to be associated with additional brain abnormalities, gender of the fetus, type of dilated ventricles, degree of ventricular dilatation, progression of VM, and symmetry, laterality [8]. Of these, the presence of ABA is believed to be most strongly associated with poor clinical outcome [11].

In our study, ABA was found in 66% of all subjects. In the 18-24 weeks’ group, ABA was found in 58.3% of subjects, and in the 25 week and above group, ABA was found in 70.6% of subjects. Previous studies of fetal VM mostly found on isolated VM, defined as VM being the only CNS finding on sonography. A recent study of isolated fetal VM reporting 147 fetuses with a 17% of risk of having ABA [3]. In that study, 9% risk of having ABA was found in the 20-24 weeks’ group with 99 fetuses and 33% risk of having ABA in the 25 week and over group with 48 fetuses. In a study of 185 fetuses in the third trimester with isolated mid VM, only 5.9% risk of having ABA was found [12]. Launay et al. reported, in a study of 61 fetuses with VM depicted by prenatal sonography [13], that MR was “more informative than sonography in 32.8% of cases”. Higher prevalence of having ABA in our study may be explained by patient selection. We did not recruit all subjects with a sonographic diagnosis of VM from our obstetricians, but rather selected subjects with VM fetus from our iuMR database. Moreover, the decision of the obstetricians in our institution to refer the subjects to iuMR examination may depend on their knowledge of brain abnormalities, and this is in turn associated with their confidence of making a definitive diagnosis solely by using prenatal sonography. After all, the current study did not intend to determine the rate of ABA missed by using prenatal sonography as in other studies, but aimed to find the prevalence of ABA in fetuses with VM identified by using iuMR examination.

Our results showed that the prevalence of having ABA increased with the degree of VM in all subjects, in the 18-24 weeks’ group, and in the 25 week and over group (Table 2). This relationship was similar to that reported by Griffiths et al. in their study of VM[3], although in their study only, which only recruited subjects with isolated VM. In our study, ABA was about three to five times more frequently found in subjects with severe VM than in subjects with mild

<table>
<thead>
<tr>
<th>Additional Abnormality</th>
<th>All</th>
<th>18-24 weeks</th>
<th>≥25 weeks</th>
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<tbody>
<tr>
<td>PVL / encephalomalacia</td>
<td>1</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>DCC</td>
<td>1</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>HPE</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>GMH</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>DWS</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Chiari malformation</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Arachnoid cyst</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Encephalo- or meningocele</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hemimegalencephaly</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Cystic tumor</td>
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<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Aqueductal stenosis</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 1. Details and distribution of additional brain abnormalities with respect to ventriculomegaly grading (1: mild, 2: moderate, 3: severe) and gestational age.
Fetal ventriculomegaly

Brain abnormalities, whether congenital or acquired, are associated with mal-development or secondary destruction of ventricles, respectively, both conditions leading to the enlargement of ventricles. This may explain why higher risk of having ABA was found in subjects with severe VM.

About 70% of ABA found in subjects with severe VM was ACC, which was slightly more common than destructive lesions (encephalomalacia/PVL). This was also compatible with the results of the previous study [3]. Obstetricians or fetomaternal experts tended to refer patients with diseases difficult to diagnose by using sonography. For instance, ACC is typically diagnosed at sonography with an abnormal ventricular configuration, but in fetuses with normal-sized or mildly enlarged ventricles, such abnormal configuration may be missed. Moreover, in fetuses with abnormal corpus callosum related to encephalomalacia but having a normal ventricular contour may again be missed at sonography. The direct visualization of the corpus callosum by using iuMR, when compared with sonography, allow a more precise diagnosis of callosal abnormalities [5].

In our cohort, most fetuses had severe VM (33/75, 44%), followed by fetuses with moderate VM (28/75, 37%), and those with mild VM (14/75, 19%). Obstetricians or fetomaternal experts may be more likely to refer patients with severe VM to iuMR examination because fetuses with mild VM were associated with low incidence of ABA [3, 12, 14]. Variations may exist among the referring physicians in that some physicians may be likely to refer fetuses to iuMR examination for a confirmation of the diagnosis, while others may only refer cases to iuMR examination when they were not confident enough to make a definitive diagnosis solely by using sonography. We did not know how severely our results were affected by this referral bias.

Several limitations may exist in this study. Referral bias, as we have previously mentioned, could not be excluded from this study. The diagnoses were not proven by pathological examination nor confirmed by postnatal imaging studies. Although pathological examination is the gold standard of diagnosis, autopsy of terminated fetuses has been a very rare practice in Taiwan. When ABA was detected, fetuses younger than 24 weeks of gestation were terminated. Because our hospital is a medical center, most of the fetuses older than 24 weeks underwent iuMR were from other institutions or clinics; when brain abnormalities were found in these fetuses, they were mostly managed in the original institutions and thus were hard to follow. However, in most cases with ABA in our study, findings of iuMR were considered to be sufficiently diagnostic. Finally, as this was a retrospective cross-sectional study, the possibility of further change of structural abnormalities of the fetuses over time could not be excluded.

CONCLUSION

In this highly selective cohort, additional brain abnormalities were shown on iuMR in 66.7% of subjects with VM, with the most common entity being corpus callosal dysgenesis. The prevalence of having ABA increases with the degree of fetal VM; subjects with severe VM have higher prevalence of having ABA when compared with subjects of mild VM. Knowing this relationship may be valuable to the interpretation of iuMR examination when the reader is faced with subjects with VM. Caution should be exercised that this trend of ABA does not apply to those fetuses with isolated VM by sonography due to the different subjects studied.

REFERENCES


Table 2 Prevalence of having additional brain abnormalities with respect to ventriculomegaly grading. The prevalence increases in all groups as the ventriculomegaly grading increases.

<table>
<thead>
<tr>
<th>VM grade</th>
<th>All (n, %)</th>
<th>18-24 weeks (n, %)</th>
<th>≥25 weeks (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>3/14, 21.4%</td>
<td>1/4, 25.0%</td>
<td>2/10, 20.0%</td>
</tr>
<tr>
<td>Moderate</td>
<td>17/28, 60.7%</td>
<td>7/12, 58.3%</td>
<td>10/16, 62.5%</td>
</tr>
<tr>
<td>Severe</td>
<td>30/33, 90.9%</td>
<td>6/8, 75.0%</td>
<td>24/25, 96.0%</td>
</tr>
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</table>
Fetal ventriculomegaly